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10/509,417	05/12/2005	Rachael Ann Ancliff	PG4791USw	5102

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EXAMINER	
LOEWE, SUN JAE Y	
ART UNIT	**PAPER NUMBER**
1609	
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05/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,417	ANCLIFF ET AL.	
	Examiner	Art Unit	
	Sun Jae Y. Loewe	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *9* is/are allowed.

6)☒ Claim(s) *1,2 and 4-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/27/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on September 27, 2004 was in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. Accordingly, the information disclosure statement was considered. A signed copy of form 1449 is enclosed herewith.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 4 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of the symptoms of asthma (Barnes, P.J., Cytokine & Growth Factor Reviews, 14, 2003, p. 516, 2nd column 2nd paragraph), does not reasonably provide enablement for the "treatment of inflammatory condition." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The breadth of the claims

The claims are drawn to a method of using the compound of formula (I) to treat inflammatory conditions. The term "treatment" is defined in the specification (p.12) to encompass prophylaxis as well as the treatment of established conditions. It is noted that "prophylaxis" is not defined in the specification, thus, the art recognized meaning will be applied for the purpose of examination: ie. the preventing of a disease (http://dictionary.reference.com/browse/prophylaxis). Furthermore, the scope of the term "inflammatory condition" is not limited by the claim or specification (p. 11). Thus, the scope extends to *all* diseases that have an inflammatory component.

The nature of the invention
The claimed compound of formula (I) has been shown to bind to the CCR3 receptor and inhibit eosinophil (an inflammatory mediator).

The state of the prior art
The scope of "diseases with an inflammatory component" is very large, as evidenced by Applicant's list on pages 11-12. This list is by far not comprehensive. A thorough discussion of the breath of the diseases encompassed is beyond the scope of this action. Thus, a few representative examples will be discussed in order to convey the low level of predictability in the art.

Each specific inflammatory disease is associated with different and often multiple mediators with redundant effects. For example, there have been more than 100 mediators identified for asthma (Barnes, P.J., Pharmacological Reviews, Vol 56, No 4, p. 517). Barnes states that "blocking a single mediator when so many are involved and with redundant effects, it is unlikely that this approach will produce major clinical benefit...the only way to determine the importance of a mediator is to study the effect of a specific inhibitor in the disease, and this will require careful and prolonged clinical studies" (Barnes, P.J., Pharmacological Reviews, Vol 56, No 4, p. 541).

In a review of mechanisms of commonly known inflammatory diseases (Luster, A.D., The New England Journal of Medicine, Vol 338, p.441), eosinophil was disclosed to be associated only with asthma and inflammatory bowel disease. Thus, a role of this mediator in other inflammatory diseases is not established in the art.

The level of one of ordinary skill and level of predictability in the art
The level of ordinary skill insufficient to overcome the low level of predictability in the art. Without specific and directed guidance in the disclosure as to how the skilled artisan may "treat" (including prophylaxis) specific inflammatory diseases, the level of skill and predictability in the art is such that a nexus cannot be established between inflammatory conditions and eosinophil inhibition (with the exception of the treatment of symptoms of asthma, see above).

The amount of direction provided by the inventor and the existence of working examples
The specification provides only the synthesis of compound of formula (I), and a statement that this compound binds to CCR3 and inhibits eosinophil.

The quantity of experimentation needed to make or use the invention
Based on the limited disclosure and the unpredictability in the art, the specification does not enable one of ordinary skill to practice the invention in claim 4 without first making an inventive step. The quantity of experimentation needed is deemed to be undue.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 1 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is drawn to "compound of Formula (I) *and* a salt or solvate thereof". It is unclear whether the invention is drawn to a *mixture* of the separate components (ie. parent compound, salt, solvate), or whether the components are *distinct inventions* within one claim. If the components are distinct inventions, they should be referred to in *alternative* form

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, 2, 4-6 rejected under 35 U.S.C. 102(e) as being anticipated by Ancliff et al. US 7,101,882.

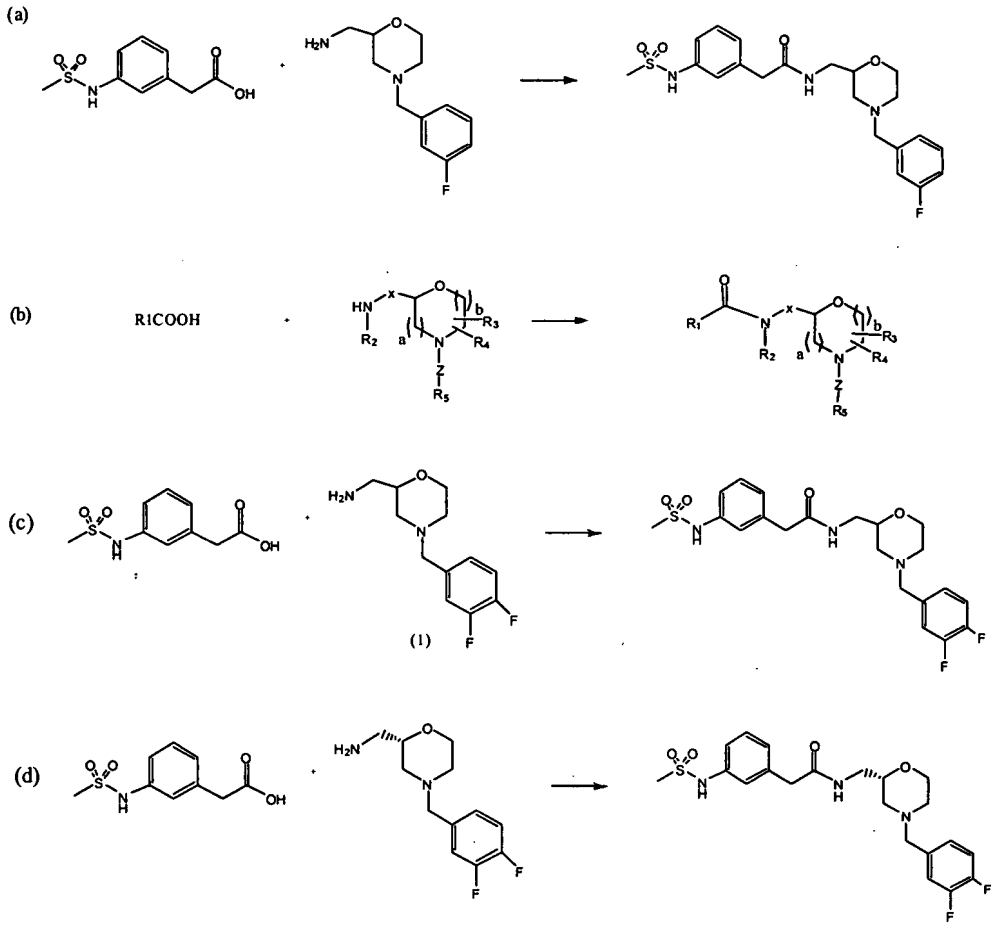
Ancliff et al. teach N-{[4-(3,4-difluorobenzyl) morpholin-2-yl]methyl}-2-{3-[(methylsulfonyl)amino]phenyl}acetamide (example 95, column 52), a pharmaceutical composition thereof (claim 16), and a method of use for treating inflammatory conditions (claim 18).

It is commonly known in the art that the synthesis of organic compounds containing a chiral carbon atom yields racemic mixtures, ie. mixtures with equal amounts of the left and right handed enantiomers (http://en.wikipedia.org/wiki/Racemic_mixture). Because N-{[4-(3,4-difluorobenzyl) morpholin-2-yl]methyl}-2-{3-(methylsulfonyl) amino]phenyl}acetamide contains a chiral carbon atom, it occurs as a racemic mixture that contains the instantly claimed 2S enantiomer. Thus, N-{[4-(3,4-difluorobenzyl)morpholin-2-yl]methyl}-2-{3-[(methylsulfonyl)amino]phenyl}acetamide anticipates N-{[(2S)-4-(3,4-difluorobenzyl)morpholin-2-yl]methyl}-2-{3-[(methylsulfonyl)amino]phenyl}acetamide (instant claim 1).

Ancliff et al. disclose that the preparation of N-{[4-(3,4-difluorobenzyl) morpholin-2-yl]methyl}-2-{3-[(methylsulfonyl)amino]phenyl}acetamide is analogous to the process shown in Scheme 1a. The reference further teaches a generic form of this

process (see Scheme 1b). Based on this information, one of ordinary skill can easily substitute the appropriate variables for a, b, z, R^1, R^2, R^3, R^4 and R^5, consistent with N-{[4-(3,4-difluorobenzyl)morpholin-2-yl]methyl}-2-{3-[(methylsulfonyl)amino] phenyl}acetamide, to arrive at the synthetic scheme shown in Scheme 1c. With the common knowledge that (1) occurs as a racemic mixture, the skilled artisan can, from Scheme 1c, deduce that this process encompasses the synthesis in Scheme 1d for the 2S enantiomer N-{[(2S)-4-(3,4-difluorobenzyl)morpholin-2-yl]methyl}-2-{3-[(methylsulfonyl)amino] phenyl}acetamide. Therefore, the reference teaches the process of instant claim 2 and the compound of instant claim 6.

Scheme 1



The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

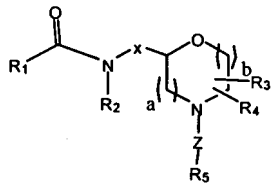
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

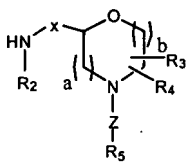
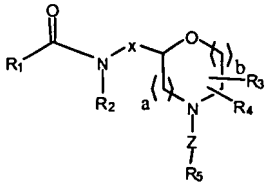
6. Claims 1, 2, 4-6 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11, 13-16, 18, 24, and 25 of U.S. Patent No. 7,101,882. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

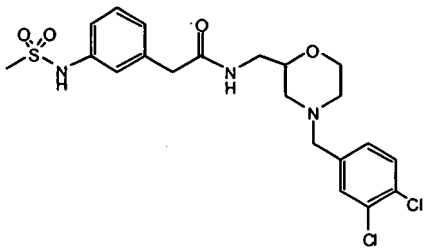
(a) Claims 15, 16, 18, 24, and 25 of U.S. 7,101,882 anticipate instant claims 1, 2, 4-6 for the reason discussed in section 5, namely N-{[4-(3,4-difluorobenzyl)morpholin-2-yl]methyl}-2-{3-[(methylsulfonyl)amino] phenyl}acetamide encompasses the instantly claimed 2S isomer.

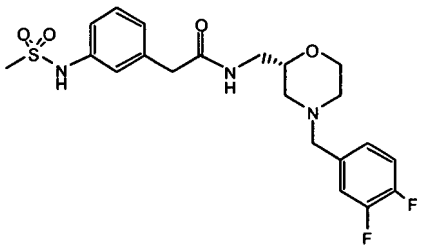
(b) Claims 1-7, 9-11, 13 and 14 in U.S. 7,101,882 are not patentably distinct from instant claims 1, 2, 4-6, see Graham v. Deere analysis below.

Scheme 2

(a) 

(b) R1COOH +  → 

(c) 

(d) 

Determining the scope and contents of claims 1-7, 9-11, 13, 14 in U.S. 7,101,882

Claims drawn to the genus of compounds in Scheme 2a, generic process of making (Scheme 2b), pharmaceutical compositions, and method of treating inflammatory conditions using these compounds.

N-{[4-(3,4-dichlorobenzyl) morpholin-2-yl]methyl}-2-{3-(methylsulfonyl) amino]phenyl}acetamide was determined to be *one* preferred embodiment, based on the limitations in the dependent claims (2-7, 10 and 11) and specific naming in claim 9, column 77, 12th entry from the bottom (see Scheme 2c).

Ascertaining the difference between claims 1-7, 9-11, 13 in U.S. 7,101,882 and the instant claims

Instant claims 1, 2, 4-6 drawn to N-{[(2S)-4-(3,4-difluorobenzyl) morpholin-2-yl]methyl}-2-{3-[(methylsulfonyl)amino]phenyl}acetamide – Scheme 2d, a pharmaceutical composition thereof, a process of making and a process of using for the treatment of inflammatory conditions.

The differences between the claimed embodiment in U.S. 7,101,882 (Scheme 2c) and the instantly claimed species are:
1) the identity of the halogen substituents to the phenyl ring: chlorine vs. fluorine
2) 2c is a racemic mixture, 2d is the 2S enantiomer.

Resolving the level of ordinary skill in the art – prima facie obviousness

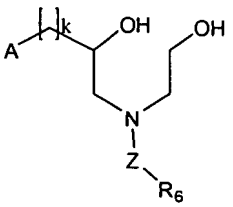
MPEP § 2144.08.II.A.4(c) states "...consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties". This is a "Genus-Species Guidelines" for the examination based on 35 U.S.C. 103. An analogous guideline was followed here for the analysis of obviousness-type double patenting.

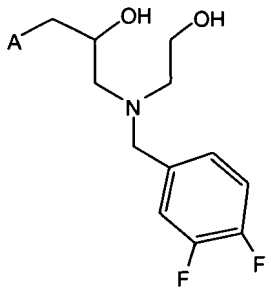
The preferred embodiment shown in Scheme 2c for U.S. 7,101,882 has very close structural similarities and similar utilities to the instantly claimed species in Scheme 2d. The skilled artisan in possession of U.S. 7,101,882 would be motivated to make the instantly claimed compound with a reasonable expectation of retaining the claimed utility. See also, *Ex parte Wiseman* (POBA 1953) 98 USPQ 277 (a difluorinated compound was held unpatentable over the prior art dichloro compound). Thus, the genus, in combination with the preferred embodiment which is patentably indistinct from the instantly claimed compound, suggests to the skilled artisan the choice of the compound in the instant claim. The instant claims are *prima facie* obvious over the claims referenced for U.S. 7,101,882.

7. Claims 7-8 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 5 of copending Application No.10/509,519. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reason provided below.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Scheme 3

(a) 

(b) 

Determining the scope and contents of claim 5 in U.S. Application 10/509519
Claims drawn to the genus of compounds in Scheme 3a, which are intermediates in a synthetic process.

One preferred embodiment for the intermediate is shown in Scheme 3b, deduced based on a reported final product N-([4-(3,4-Difluorobenzyl)morpholin-2-yl] methyl}-2-{4-[(methylsulfonyl)amino]phenyl}acetamide (Example 45, page 51, synthetic steps disclosed on pages 29, 33, 50, 51) by substituting the specific k, Z and R^6 variables from this product into formula of Scheme 3a.

Ascertaining the difference between claim 5 in U.S. Application 10/509,519 and the instant claims
Instant claims 7 and 8 drawn to the compounds that are, respectively, the racemic mixture and an enantiomer of the racemate shown inn Scheme 3b.

Resolving the level of ordinary skill in the art – prima facie obviousness
MPEP § 2144.08.II.A.4(c) states "...consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that

structurally similar species usually have similar properties". This is a "Genus-Species Guidelines" for the examination based on 35 U.S.C. 103. An analogous guideline was followed here for the analysis of obviousness-type double patenting.
Based on the implicit disclosure of the compound in Scheme 3b, which anticipate the compounds in the instant claims, one of ordinary skill would find the motivation to pick the latter from the genus claimed in U.S. Application 10/509519. Thus, the instant claims are *prima facie* obvious over claim 5 in U.S. Application 10/509,519.

Allowable Subject Matter

8. Compound of formula V (claim 9) is allowable over the prior art for the following reason. The closest art is 2-(3,4-Dichlorobenzylamino)-ethanol taught by, for example, Ancliff et al. (U.S. 7,101,882). Although the structures of the prior art and the instant claims are similar, the utilities are different. Namely, compound V is an essential intermediate in the instant synthesis of compound of formula I. Thus, the motivation to modify the prior art compound to arrive at the instant structure of compound V is not available to one of ordinary skill.

Conclusion

9. Claims 1, 2, 4-8 rejected. Claim 9 allowable.

10. Any inquiry concerning this communication should be directed to Sun Jae Y. Loewe whose telephone number is 571-272-9074. The examiner can normally be reached on Monday through Friday from 7:30 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Cecilia Tsang (571) 272-0562, can be reached. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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